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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,396	01/16/2002	Denis Labrecque	108184-00017	3427
24999	7590	10/20/2003	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, PC 2200 CLARENDON BLVD SUITE 1400 ARLINGTON, VA 22201			SMALL, ANDREA D SOUZA	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/046,396	LABRECQUE ET AL.	
	Examiner	Art Unit	
	Andrea D Small	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16, 18-19, 22-34, 36-37 and 40-75 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16, 18, 19, 22-34, 36, 37 and 40-75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

I. Applicants Response:

Applicants response filed 8/22/2003 has been received and entered into the file.

II. Amendments:

- (a) Cancelled claims: 17, 20, 21, 35, 38 and 39.
- (b) Pending claims: 1-16, 18-19, 22-34, 36-37 and 40-75.

III. Remarks:

- (a) Issues under 35 USC 112(1):

Claims 1-16, 18-19, 22-34, 36-37 and 40-75 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1 and 27 had incomplete molecules due to the dangling valences found on the molecules, the divalent nitrogen, the monovalent oxygen, and when G2 is a non-heterocycle, the divalent nitrogen or the monovalent oxygen or sulfur on the molecule. The “how to make” requirement of 35 USC §112, first paragraph has not been met as the application offered no method for preparing an incomplete molecules. Applicants have attempted to obviate the above rejection by inserting NH for the A1 and A2 moieties; NH for the A3 moiety and NH₂ and –NH-G2 forms a urea moiety for the A4 moiety. These amendments have not been found to be sufficient to overcome the rejected as cited supra. There are still moieties within the molecular formula depicted in claim 1 that have dangling valences that have not been fulfilled such as the oxygen moieties that are at the end of the molecule. Thus, this rejection is maintained.

(b) Issues under 35 USC 112(2): Claims 1-16, 18-19, 22-34, 36-37 and 40-75 were rejected as being indefinite as the molecules depicted in claim 1 are incomplete with regard to the dangling valences such as the oxygen moieties at the end of the molecule which mono-valence is not fulfilled. Therefore, this rejection is maintained.

(c) Issues under 35 USC 112(1), objections and 112(2) with regard to new matter situation and lacking antecedent basis respectively: The cancellation of the phrase “the valences of each O, N or S are adjusted by adding a H if needed” has overcome these rejections.

IV. Maintained Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(a) Claims 1-16, 18-19, 22-34, 36-37 and 40-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1 and 27 have incomplete molecules due to the dangling valences found on the monovalent oxygen on the molecule. The “how to make” requirement of 35 USC §112, first paragraph has not been met as the application offers no method for preparing an incomplete molecule in claims 1 and 27 to complete the dangling valences.

Support is seen only for the specific compounds of the elected area in the examples which are, examples VII, VIII, IX, X, XI, XVIII, XIX, XXI, and XXX.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(a) Claims 1-16, 18-19, 22-34, 36-37 and 40-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 27 have incomplete molecules due to the dangling valences found on the molecule such as the monovalent oxygen, on the molecule. The above molecule is incomplete and thereby allows for varying possibilities of substituents to be attached on the molecule.

V. New Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(a) Claims 1-16, 18-19, 22-34, 36-37 and 40-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants have amended claims 1, 4, 6, 16, 18, 19, 27, 34, 36 and 37 by reciting definitions for A3, A4, NH-G2 and X that have no descriptive support in the specification to support a genus wherein all compounds of the formula in claim 1 could have possibilities for substitution where A3 is NH, A4 is NH₂, NH-G2 and X is NH. These

substituents find support in specific compounds such as those discussed in Applicants remarks. However, these substitutions on those specific compounds do NOT provide sufficient description to support the entire genus as instantly claimed. Applicants assert that "...that the disclosure as filed reasonably conveys possession of the claimed subject matter. See, e.g., *In re Kaslow*, 217 USPQ 1089 (Fed. Cir. 1982). *Ipsis verbis* disclosure is not required. See, e.g., *Fujikawa v. Wattanasin*, 39 USPQ 1895 (Fed. Cir. 1996)."

Applicants assertion is well taken, but as the court in *Fujikawa* reasoned that despite the fact that *ipsis verbis* disclosure is not required, "just because a moiety is listed as one possible choice for one position does not mean there is *ipsis verbis* support for every species or sub-genus that chooses that moiety. Were this the case, a description "laundry list" disclosure of every possible moiety for every possible position would constitute a written description of every species in the genus. This cannot be because such a disclosure would not "reasonably lead" those skilled in the art to a particular species." By analogy, the instant description provides one or two possible moieties that have their valences fulfilled in the manner instantly claimed, for example the exemplified compounds VII, VIII, IX, X, XI, XVIII, XIX, XXI, and XXX; however, these moieties do not support a genus where for instance, X is N or G4 is arylamino or G1 is absent, etc. The support Applicants seek from the disclosure does not "reasonably lead" those skilled in the art to the particular genus as instantly claimed, let alone a particular species within the genus. The knowledge generally available to an ordinary skilled artisan does not overcome the fact that there are many means by which the genus as claimed could have its valences fulfilled. Thus, the amendments as indicated supra are determined to be new matter. See *Ex parte Fox*, 128 USPQ 157, 1960 C. D. 28, 761 O. g. 906 (Bd. App. 1957).

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(b) Claims 42, 43, 58, 59 and 75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for solid tumor cancer such as breast, prostate, lung, colon, ovary, etc, does not reasonably provide enablement for all tumors or cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification does not give any guidance as to the full range of tumors or cancers which could be treated using the instant claimed compounds. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention:

The invention is a treatment of cancers and tumors by administering to a patient in need thereof a compound or composition containing the compound according to claim 1.

2. the state of the prior art:

The state of the prior art is such that there are a variety of treatments for cancers depending on the class the cancer or tumor falls within, such treatments include:

- (1) alkylating agents which are useful in treating prostate cancer, lung cancer, breast cancer and the like;
- (2) anti-metabolites, which are used to masquerade as building blocks of DNA which prevent DNA from replicating resulting in death to the cell;
- (3) plant alkaloids which inhibit cell division and prevent formation of the microtubules critical for mitosis;

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(4) antitumor antibiotics, which block cell division by binding DNA and preventing the double helix from unwinding for replication, etc.

3. the predictability or lack thereof in the art:

There is a very low level of predictability with regard to cancer or tumor treatments across the spectrum of cancers which are now known and classified because each class of cancer or tumor varies extensively. The differences in nuclear morphology, the variance in phenotype, the variance in clustering of the cells all lead to variance in the approaches used to treat the various classes of cancer or tumors. There is also a lack of predictability of causative agents for various cancers, some are a result of hereditary influence, environmental factors, others are biochemically induced, etc. All these variances lead to the predictability of one drug being able to treat the numerous types and classes of cancers or tumors being slim to none.

4. the amount of direction or guidance present:

The direction or guidance present in the instant disclosure is that to treatment of some solid tumor cancers such as lung cancer. There is very little guidance provided as to the extrapolation capabilities of the data to other types of cancer or tumors.

5. the presence or absence of working examples:

The examples provided to the cross-section of cancers or tumors contemplated by the instant claims are very few.

6. the breadth of the claims:

The claims as instantly recited are very broad and reach through to cancers that are not enabled by the instant disclosure.

7. the quantity of experimentation needed:

The quantity of experimentation needed would cause an undue burden on the ordinary skilled artisan. They would have to determine which classes of cancers or tumors the results of the instant disclosure could be extrapolated to, following which mechanisms for such extrapolation would have to be contemplated and designed, in-vivo and in-vitro tests would then have to be employed to determine if in fact the compounds as claimed could treat all the cancers or tumors that are encompassed by the instant claims; and

8. the level of the skill in the art.

The level of skill in the art is such that without more guidance or predictability assays one of ordinary skill in the art would have an undue burden placed on him/herself to practice the invention as claimed to the scope contemplated.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

- (a) Claims 1-16, 18-19, 22-34, 36-37 and 40-75 recites the limitation a genus wherein all compounds of the formula in claim 1 could have possibilities for substitution where A3 is NH, A4 is NH₂, NH-G₂ and X is NH. There is insufficient antecedent basis for this limitation in the specification or originally filed claims.
- (b) Claims 1-16, 18, 22-34, 36 and 40-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 and 27 recite where A3 is NH and A4 is NH₂, this provides for a moiety N=NH-NH₂, which is chemically impossible because it leads to the middle

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N atom having 4 valences rather than the three that is chemically possible, therefore, these substituents render the claim indefinite.

(c) Claims 18 and 36 recites the limitation "wherein NH-G2 forms a guanidine moiety" in 1 and 27 respectively. There is insufficient antecedent basis for this limitation in the claim, as the claim does not recite where NH-G2 forms a guanidine moiety.

VI. Objections:

The amendment filed 8/22/2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: A3 is *NH*, A4 is *NH2*, *NH-G2* and X is *NH*.

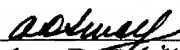
Applicant is required to cancel the new matter in the reply to this Office Action.

VII. Contact Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrea D. Small whose telephone number is (703) 305-0811.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:30-6:30 PM. The number for accessing the facsimile machine is (703) 746-4984.



Andrea D. Small, Esq.
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

October 14, 2003